Hong Kong College of Physicians
Case Report for Interim Assessment
Specialty Board of Advanced Internal Medicine (AIM)

For AIM Training, case reports should be submitted in the prescribed format together with the application form for Interim Assessment at least EIGHT Weeks before the date of Interim Assessment

Name of candidate (print and sign):
Hospital and Unit: Specialty:
Name of supervisor (print and sign):
Date(s) and place (hospital) of patient encounter: 2/2020 and 3/2020
Date of report submission: 7/9/2021

Case report

Note: Failure to follow the prescribed format (including the number of words) results in a FAILURE mark (score between 0 and 4) for the Case Report.

Title: A case of normal pressure hydrocephalus presenting with frequent falls

Case history:

An 86-year-old gentleman was admitted with recurrent falls in 2/2020. He had a past medical history of hypertension, hyperlipidaemia, hypothyroidism, benign prostatic hypertrophy and prostatic carcinoma for conservative management. He attended the emergency department in 1/2020 for fall, and had another fall prior to this admission for which he did not seek medical attention. He managed to walk with a quadripod after his first fall, but his mobility gradually declined. He fell on this occasion while trying to stand from a sitting position. He was confused on admission, but examination was otherwise unremarkable. He was found to have a urinary tract infection and was treated with a course of antibiotics. Computed tomography of the brain (CTB) showed small vessel disease. Blood tests for Vitamin B12 and Venereal Disease Research Laboratory test (VDRL) were negative. Folic acid was added in view of low serum folate; thyroxine dose was increased in view of sub-optimally controlled hypothyroidism. He completed a course of rehabilitation, managing to walk with a frame with assistance for a short distance upon discharge.

He was re-admitted 2 weeks with another fall while shopping in a mall alone. He was disorientated when approached by the mall staff. Collateral history from his son revealed

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deteriorating cognition since 1/2020. Examination showed no focal neurology nor signs of parkinsonism, but a small-step gait with fair stability and balance was noted. A repeat CTB showed prominent ventricles with mild ballooning that was slightly disproportionate to sulcal space age-related changes. The Evans' ratio (ratio of the maximal frontal horn ventricular width and the maximal inner diameter of the skull at the same axial plane) was raised (image 1). He scored 8/30 on the Montreal Cognitive Assessment Hong Kong (HK-MoCA), scoring particularly poorly on visuospatial and executive function, abstraction, attention and delayed recall. In view of the clinical history and CTB findings, idiopathic normal pressure hydrocephalus (iNPH) was suspected. A tap test was done, with 30ml of cerebrospinal fluid (CSF) drained via lumbar puncture. The opening pressure was normal, CSF biochemistry and culture were unremarkable. There was marked improvement in mobility and cognitive function following the test. The patient was able to walk with a frame with stand-by to mild assistance from 2 therapists for 50m pre-test. He was able to walk with a stick with minimal to mild assistance from 1 therapist for 50m post-test. The HK-MoCA improved to 12/30, particularly in attention and orientation. A Magnetic Resonance Imaging (MRI) CSF flow study was arranged and the patient was referred to the neurosurgeons for possible iNPH.

He was admitted under the neurosurgical team in Queen Elizabeth Hospital in 6/2020 with a repeat tap test done. Pre- and post-test assessment results were unfortunately unavailable. He subsequently underwent surgery for a right ventriculoperitoneal (VP) shunt with a programmable valve. He developed a subdural haematoma (SDH) few weeks post-surgery, requiring tuning up of his valve setting. He completed a course of rehabilitation, managing to walk with a stick with slight assistance for 30m. Serial CTB showed resolution of SDH in 12/2020.

His mobility and cognition unfortunately declined, with repeated admissions for fall in 1/2021 and 3/2021. MRI CSF flow study in 4/2021 showed the VP shunt catheter was in situ, with known hydrocephalus and dilated lateral and third ventricles. In view of his clinical deterioration, the valve setting was tuned back down to its initial setting by the neurosurgeons in 4/2021. Despite so, his mobility and cognition remained poor despite a prolonged course of rehabilitation, ultimately requiring old age home care.

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Discussion and literature review

Normal pressure hydrocephalus is a potentially reversible disease characterised by ventriculomegaly on imaging, and a triad of gait disturbance, cognitive impairment and urinary incontinence. It can be idiopathic as seen in our case, or secondary due to intracranial haemorrhage, meningitis or brain tumour. iNPH accounts for 6% of dementia and increases with age, with a prevalence of 5-6% in octogenarians (1).

Pathophysiology

The underlying mechanism leading to iNPH is unknown. It is thought that increased CSF leads to compression of the brain, resulting in cerebral hypoperfusion (2). The frequent co-existence of iNPH with vascular dementia and Alzheimer's disease (AD) leads to the postulation that cerebrovascular events reduce vascular compliance causing compression of brain tissue. Cerebral hypoperfusion seen in vascular dementia may in turn reduce CSF turnover, resulting in accumulation of toxic proteins seen in AD (1).

Clinical presentation

The complete triad of symptoms is not essential in iNPH. In fact, only 60% of the cases have all three symptoms (3), and symptoms tend to progress over 3 to 6 months as seen in our patient (4).

Gait disturbance is often the first or most severe symptom. Patients presenting without gait disturbance should prompt consideration of an alternative diagnosis. The gait disturbance in iNPH is described as a higher-level gait disorder, in which the brain is unable to incorporate proprioceptive information into generating a normal gait (4). The gait is a symmetrical, broad-based gait with externally rotated feet, typically short-stepped and glue-footed. Patients have difficulties getting up from sitting down as seen in our patient (1). Falls are due to instability, impaired balance and postural reflexes. Objective tests, such as the Timed Up and Go (TUG) test, can be useful in gait assessment.

Cognitive impairment is mainly due to subcortical frontal dysfunction. Executive function including problem solving and processing is affected first, impacting day-to-day living even at an early stage. Attention and verbal frequency are also impaired, with slowing and worsening precision of fine motor skills. Short-term memory is also impaired, with individuals capable of encompassing new information but unable to repeat it (1). This is in keeping with the pattern of cognitive impairment seen in our patient. Conversely, recognition memory is preserved; agnosia and apraxia should prompt consideration of an alternative cause of cognitive impairment (4). Depression is common in iNPH, but behavioural and psychological symptoms of dementia is less common than in AD (3). Mini-mental state examination and HK-MoCA are

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useful screening tests, and tests specific for subcortical impairment including the grooved pegboard test and trail-making A/B tests can be helpful (1).

iNPH patients often present with urgency and frequency before progressing to incontinence. 70% patients are found to have detrusor hyperactivity (3). On the other hand, faecal incontinence is uncommon and if present, indicates severe subcortical frontal dysfunction.

Differential diagnosis of iNPH

It can be difficult to distinguish iNPH from other diagnoses as concomitant vascular dementia or AD occurs in 75% of cases (1). In a retrospective study of 142 iNPH patients with shunting done, 24% showed neuropathological changes of AD (5). There are many overlapping clinical features, but gait disturbance tends not to occur until at least moderately severe AD. Asymmetrical symptoms and evidence of cerebrovascular events on neuroimaging may help differentiate iNPH from vascular dementia.

Parkinson's disease is also an important differential diagnosis. A population study shows that 71% of iNPH patients have features of parkinsonism, most common being bradykinesia and postural instability. Tremor is uncommon (5%), and the asymmetry of symptoms in parkinsonism can help differentiate between the two (6). Unlike parkinsonism, mobility in iNPH patients does not improve with cues or visual landmarks (3). Nevertheless, it is difficult to differentiate the two based on clinical features alone and neuroimaging can be helpful.

Diagnosis

There is no gold standard for diagnosing iNPH. Neuroimaging features and CSF tap test are used to support the diagnosis in patients with compatible symptoms.

Both computed tomography (CT) and MRI can demonstrate ventriculomegaly, but MRI is superior in showing other features. iNPH patients exhibit neuroimaging findings of DESH, that is ventriculomegaly and narrowing of subarachnoid space at cerebral high convexities (3). Ventriculomegaly is a key finding and is defined by an Evans' ratio of >0.3. This can also be seen with age and other neurodegenerative disorders. Other features of DESH, including Sylvian fissure enlargement and shrinkage of high convexity or midline subarachnoid space, are more sensitive and specific in distinguishing iNPH from other causes of ventriculomegaly. A callosal angle of <90^{o} (angle between the lateral ventricles on coronal images) is an indirect index of DESH and can help differentiate iNPH from AD. Periventricular white matter hyperdensities are seen in patients with severe iNPH, but can also be attributed to other causes, such as cerebral amyloid angiopathy which may be associated with AD (7).

A CSF tap test involves removing 30-50ml CSF and performing pre- and post-assessments on symptoms. Surgical treatment is usually considered if there is marked improvement in mobility, as few patients show immediate cognitive improvement (2). However, a lack of response does not exclude iNPH as it is more specific (75%) than sensitive (58%) (3). A CSF drainage test can be done in place of a tap test, in which CSF is drained at 10mls/hour via a spinal catheter over 72 hours with assessments done before and during drainage. Alternatively, a CSF infusion test can be done by infiltrating the CSF space with Ringer's lactate via a spinal catheter and measuring CSF outflow resistance (R_{out}) with a second catheter. An increased R_{out} predicts a better surgical outcome (1).

There is great interest in finding a CSF biomarker for iNPH. Although there is currently no specific marker for diagnosing iNPH, it has been suggested that a low amyloid $\beta 42$ and high total tau levels correlate with poorer post-shunting outcomes. As these markers rise shortly after surgery, they are of less diagnostic value in detecting co-existing AD (7).

Ventricular shunting and outcomes

Shunt surgery remains the mainstay of treatment. This usually involves a VP shunt, but lumbo-peritoneal and rarely ventriculo-atrial shunts are also performed. Programmable shunts are commonly used as they allow the opening pressure to be adjusted to control the level of drainage, as seen in our patient. Complications of VP shunt include shunt failure, infection and over-drainage. Patients with over-drainage may experience low pressure symptoms, such as postural headache and muffled hearing. They should therefore be monitored with intermittent imaging in the first 6-12 months post-surgery to look for subdural haematoma or effusion which are signs of over-drainage. Significant ventricular narrowing on ventricles does not correlate with clinical outcome but instead represents over-drainage. Such findings necessitate an increase in shunt setting and further monitoring as seen in our patient.

The response rate to shunt surgery is 63-84% at 1 year and 60-74% at 2 to 6 years (3). A retrospective study found that the negative predictors at 1-year follow-up included age $\geq$80years, history of cerebrovascular accidents, longer waiting time till surgery, and shunt complications (8). Patients undergoing shunt surgery who experience clinical improvement tend to range between 70 to 80 years of age, thus it is not known if the same benefits translate to an older age group. Given our patient's age and post-operative shunt complication of an SDH, this might explain why he deteriorated within the first year of shunt surgery. Nevertheless, age alone should not be a deterrent to surgery as 39% of patients over 80 years improve after shunting (8).

Another explanation for our patient's deterioration post-surgery could be other previously

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undiagnosed neurodegenerative disease. As elucidated, it can be difficult to differentiate iNPH from other neurodegenerative disorders and they can often co-exist. In a study looking at post-shunting outcomes in patients with iNPH versus iNPH and biopsy-proven AD, improvement and complete resolution of symptoms were significantly higher in the iNPH cohort compared with the iNPH plus AD group (54% versus 30%). Even in subjects who showed improvement post-tap test, only 18% of those with iNPH and AD improved post-shunting, compared with 45% of those with iNPH alone (5).

Future research

Despite iNPH being first described over 50 years ago, there is still much unknown about the mechanisms underpinning its clinical symptoms. Future research on pathophysiology may facilitate identification of specific markers to aid diagnosis and differentiation from other diseases. Given the current lack of a diagnostic gold standard, a more standardised assessment to quantify improvement following CSF tap or drainage tests is necessary to allow better comparison between different studies. This will allow better patient selection for shunt surgery.

Tables and figures (where applicable) (no more than two figures)

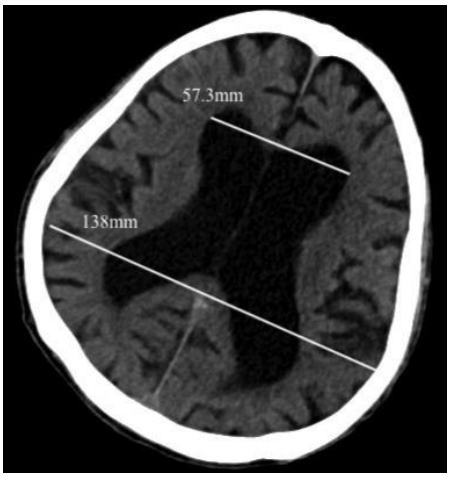

Image 1. Plain computed tomography of the brain showing an Evans' Ratio >0.3

Reference (not more than 10)

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No of words in Case History and Discussion (excluding references):____1997_____.

(should be between 1000-2000)

Declaration

I hereby declare that the case report submitted represents my own work and adheres to the prescribed format. I have been in clinical contact with the case selected. The case report has not been submitted to any assessment board or publication and it is NOT related to my second specialty(ies), if any. My consent is hereby given to the College to keep a copy of my case report, in written and/or electronic, at the College Secretariat and allow the public to have free access to the work for reference.

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(signature of Trainee)

Endorsed by Supervisor *

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